

Remarks

Addressing the Examiner's Rejection of the Claims Under 35 U.S.C. §103(a)

The Examiner has rejected claims 1-34 under 35 U.S.C. §103(a) asserting that the claims are obvious over Kurnik (WO 99/58973) in view of Tamada, et al. (JAMA 282(19):1839-1844, 17 November 1999).

The PTO has the burden of establishing a case of *prima facie* obviousness and can meet this burden “only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references.” *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988).

Applicants respectfully traverse the Examiner's rejection of the claims for the following reasons. The present invention relates to a multiple step approach to predicting a hypoglycemic event in a subject when **both** (i) comparing the predicted glucose measurement value to the threshold glucose value indicates a hypoglycemic event at the further time interval, **and** (ii) comparing the skin conductance and/or temperature value or trend of skin conductance and/or temperature values with the threshold skin conductance and/or temperature value indicates a hypoglycemic event.

Kurnik teaches a method and device for predicting a future or past concentration of an analyte using a series of measurements obtained from a monitoring system. One application of the teachings of the Kurnik reference involves predicting future or past blood glucose concentrations (see, e.g., Kurnik, page 1, lines 6-12.) In one particular aspect of the Kurnik reference, a raw signal is obtained using a transdermal sampling system that is placed in operative contact with a skin or mucosal surface of a biological system (see, e.g., Kurnik, page 3, lines 22-25). It is only in the context of a monitoring system comprising an exemplary transdermal sampling device (i.e., an iontophoretic glucose sampling device) that skin conductance and temperature are discussed in the Kurnik reference.

The teachings concerning both perspiration and temperature in the Kurnik reference are “(i)n the context of the iontophoretic glucose sampling device described hereinabove” (Kurnik, page 42, lines 30-31). These teachings relate only to variables, including sweat and temperature, that may affect the functioning and accuracy of the iontophoretic glucose

sampling device. The Kurnik does not relate these variables to prediction of a hypoglycemic event at a future time. For example, noting that perspiration contains glucose (Kurnik, page 43, line 7), the Kurnik reference states the following:

For example, perspiration contains glucose, and perspiration occurring rapidly and in sufficient quantities **may affect the detected signal either before or during biosensor measurement** (emphasis added; Kurnik, page 43, lines 7-10).

This interpretation of the reference is confirmed by the following teaching in the Kurnik reference:

The housing 32 can further include an optional temperature sensing element (e.g., a thermistor, thermometer, or thermocouple device) which monitors the temperature at the collection reservoirs **to enable temperature correction of sensor signals**. The housing can also include an optional conductance sensing element (e.g., an integrated pair of electrodes) which monitors the conductance at the skin or mucosal surface **to enable data screening correction or invalidation of sensor signals** (emphasis added; Kurnik, page 32, line 28, to page 33, line 5).

In *Bausch & Lomb v. Barnes-Hind/Hydrocurve* (796 F.2d 443, 230 USPQ 416 (Fed. Cir. 1986)), the U.S. Court of Appeals for the Federal Circuit emphasized the following:

It is impermissible within the framework of section 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art.

The Kurnik reference neither teaches nor suggests a multiple step approach to predicting a hypoglycemic event in a subject that includes **both** (i) comparing the predicted glucose measurement value to the threshold glucose value to indicate a hypoglycemic event at the further time interval, **and** (ii) comparing the skin conductance and/or temperature value or trend of skin conductance and/or temperature values with the threshold skin conductance and/or temperature value to indicate a hypoglycemic event.

The reference of Tamada, et al., does not make up for any of the shortcomings of the Kurnik reference relative to the presently claimed invention. The reference of Tamada, et al., does not contain any teaching or suggestion of using a predicted measurement value at a further time interval to reduce the risk of hypoglycemia. The teachings of Tamada, et al.,

relate only to glucose values obtained in real time monitoring, i.e., glucose measurement values provided by GlucoWatch® (Cygnus, Inc., Redwood City, CA) biographer. The GlucoWatch biographer taught by the Tamada, et al., reference did not provide predicted glucose values at future time points. The teachings of Tamada, et al., relate to alarms based on **measured**, not predicted, glucose values (see, for example, Tamada, et al., page 1839, col. 1, second full paragraph). At page 1839, Tamada, et al., teach the following (emphasis added):

Automatic readings also provide the opportunity for an alarm to be sounded in response to values below a user-selected alert level or as a result of rapid declines in the **measured** glucose values. These alarms could provide a method to reduce the risk of hypoglycemia and make intensive therapy for diabetes safer and acceptable to more patients.

Further, the reference of Tamada, et al., does not contain any teaching or suggestion of combining a predicted glucose value from a further time interval with skin conductance or temperature threshold parameter values associated with hypoglycemia. Similarly to the teachings of the Kurnik reference, the reference of Tamada, et al., discusses skin conductance and temperature values as they affect sensor function in the monitoring device. In this regard Tamada, et al., teach the following:

Calculation of Glucose Value

The biographer contains sensors to measure skin temperature and conductance. The latter is directly related to the amount of sweat on the skin's surface. **Since the glucose in sweat can confound the measurement, if the skin conductance exceeds a predetermined threshold, the measurement for that cycle is skipped.** An alarm is sounded for both sweating and for hypoglycemia because the former is often associated with the latter. Similarly, **since temperature directly affects the sensor operation**, if the temperature or time rate of change of the temperature exceeds predetermined thresholds, the entire (measurement) cycle is skipped. (Tamada, et al., page 1841, col. 1, first full paragraph.)

Accordingly, the reference of Tamada, et al., teaches no more than the reference of Kurnik and therefore does not make up for any of the shortcomings of the Kurnik reference relative to the presently claimed invention. The reference of Tamada, et al., does not contain

any teaching or suggestion of using a multiple step approach for the prediction of hypoglycemic events (e.g., predicting a hypoglycemic event in a subject by **both** (i) comparing the predicted glucose measurement value to the threshold glucose value indicates a hypoglycemic event at the further time interval, **and** (ii) comparing the skin conductance and/or temperature value or trend of skin conductance and/or temperature values with the threshold skin conductance and/or temperature value indicates a hypoglycemic event), nor does the reference provide any reasonable expectation of success for such an approach. In fact, the reference of Tamada, et al., defaults to the use of a single alarm for both sweating and possible hypoglycemia based solely on the presence of unacceptable levels of sweat (“An alarm is sounded for both sweating and for hypoglycemia because the former is often associated with the latter”). The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaack*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Finally, even if, *in arguendo*, the elements of the present invention were taught in the prior art, the U.S. Court of Appeals for the Federal Circuit in *Symbol Technologies, Inc. v. Opticon, Inc.*, 935 F.2d 1569, 19 USPQ2d 1241 (Fed. Cir. 1991) stated the following:

We do not pick and chose among the individual elements of assorted prior art references to recreate the claimed invention, but rather, we look for some teaching or suggestion in the references to support their use in the particular claimed combination.

Prior to the teachings of the present specification, there was no indication in the cited prior art that one of ordinary skill in the art would chose a multiple step approach to predicting a hypoglycemic event in a subject that included **both** (i) comparing the predicted glucose measurement value to the threshold glucose value to indicate a hypoglycemic event at the further time interval, **and** (ii) comparing the skin conductance and/or temperature value or trend of skin conductance and/or temperature values with the threshold skin conductance and/or temperature value to indicate a hypoglycemic event. Obviousness requires some logical reason for combining the references at hand; otherwise, the use of the references will entail prohibited hindsight. See, for example, *In re Fine*, 837 F.2d 1071, 5 USPQd2 1596 (Fed. Cir. 1988); *In re Sernaker*, 702 F.2d 989, 217 USPQ 1 (Fed. Cir. 1983). Applicants

respectfully submit that no motivation to combine the references, other than hindsight reconstruction, has been supplied by the Examiner.

Further, applicants respectfully submit that the Examiner has not considered the claims “as a whole” as required for a determination of obviousness:

The '315 patent specifically stated that it disclosed and claimed a combination of features previously used in two separate devices. That fact alone is not fatal to patentability. The claimed invention must be considered as a whole, and the question is whether there is **something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination** (emphasis added). *Lindermann Maschinenfabrik GmbH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 221 USPQ 481, 488 (Fed. Cir. 1984).

Nothing in the cited references provides a teaching or suggestion of combining the elements of the claimed invention. There must be some teaching or suggestion in the cited references of the desirability of the modifications suggested by the Examiner.

Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination. Under section 103, teachings of references can be combined *only* if there is some suggestion or incentive to do so. (quoting *ACS Hosp. Systems, Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984)). . . . The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification. *In re Fritch*, 972 F.2d 1260, 23 USPQ 2d 1780, 1783–84 (Fed. Cir. 1992).

In view of the arguments presented above, applicants submit that the Examiner has failed to establish a case of *prima facie* obviousness. Accordingly, applicants respectfully request that the rejections under 35 U.S.C. §103 be withdrawn.

Conclusion

Applicants submit that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

Please direct all further communications in this application to:

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If the Examiner notes any further matters that the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned at (650) 599-3591.

Respectfully submitted,

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